Inflammatory Bowel Disease
New treatments for Crohn’s disease and ulcerative colitis

Novel approaches may provide potential breakthroughs to treat the more than 1 million Americans—more than half of them women—with inflammatory bowel disease (IBD). These strategies include less-frequent drug dosing, experimental therapies to attack some of the processes involved in IBD, and bone-sparing medications.

IBD, which includes Crohn’s Disease and Ulcerative Colitis (UC), “stems from a bacterial trigger which sets up an uncontrolled immune response in susceptible people, which in turn leads to chronic inflammation that eventually breaks down the lining of the intestines,” explains gastroenterologist Ellen Scherl, MD, an assistant professor of medicine at the Weill Medical College of Cornell University. Key symptoms include bloody diarrhea, weight loss, abdominal pain, cramps, bloating, and constipation. “Women with abdominal pains are frequently told they have ovarian cysts and undergo unnecessary procedures, when they really have Crohn’s,” says Dr. Scherl. Women are more likely than men to report more severe symptoms and sexual problems, including painful intercourse. Postmenopausal women with IBD also have a higher than normal risk for osteoporosis because their disease hinders absorption of bone-enriching calcium and vitamin D, and drugs used to control symptoms can thin bones.

**Easier to take**
As with many gastrointestinal (GI) problems, the first step in controlling symptoms is to make simple lifestyle changes (see What You Can Do, pg 5). When that’s not enough, most IBD patients are helped by drugs. Trouble is, half of them don’t take their medicine, mostly because of too-frequent dosing, says Sunanda Kane, MD, assistant professor of medicine at the University of Chicago. Once-a-day dosing may help change that.

A once-daily dose of the IBD drug mesalamine (Asacol) was found to be comparable to conventional twice- or three-times daily dosing for ulcerative colitis patients in remission, Dr. Kane reported to the American College of Gastroenterology annual meeting in October 2002. In a small pilot study of 22 ulcerative colitis patients who had no symptoms for at least six months, nearly 90 percent of those given once-daily doses for six months kept taking their medicine as prescribed, compared to only 76 percent of those taking several daily doses. Dr. Kane has begun a large, randomized trial to further test once-daily mesalamine. “Ultimately, more patients may be able to take more medication in a more convenient way,” says Dr. Kane, who is also president of “We Care in IBD,” a professional organization of specialists in treating Crohn’s and ulcerative colitis.

**New treatments ahead**
The IBD Center at Cornell headed by Dr. Scherl is taking part in several major clinical trials. One trial compares the efficacy of Asacol and balsalazide (Colazal), a newer version of mesalamine that works quickly and helps hard-to-treat cases of ulcerative colitis. The drug infliximab (Remicade) is also being tested in UC. For patients with Crohn’s disease, the IBD center is also studying high-dose regimens of Asacol, antibiotics, and a new version of a drug to block the inflammatory cytokine tumor necrosis factor alpha (TNF-α).

Other new treatments now in development show promise, investigators told the gastroenterology meeting. A small randomized trial of 23 ulcerative colitis patients found that 45 percent of those who took a highly concentrated soybean byproduct went into remission, compared to 8 percent in the placebo group, reported Gary Lichtenstein, MD, associate professor of medicine at the University of Pennsylvania. The drug, a protease

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**INFLAMMATORY BOWEL DISEASE**
The inflammation of Crohn’s disease and ulcerative colitis attacks the lining of the intestines, speeding up the normal passage of food, causing diarrhea. Malabsorption can cause weight loss and deficiencies in protein, vitamin B12, calcium and vitamin D (leading to osteoporosis). Inflammation and erosion of the intestinal lining causes ulcerations or cracks (fissures) that can bleed, causing blood in the stool (in severe cases it can lead to anemia). The wall of the intestines also becomes thickened and narrowed; in some cases, this can block food passage (strictures). Inflammation can also spread outside the bowel wall, penetrating adjacent areas and causing sections of bowel to stick together (adhesions). In some cases, a tunnel-like opening called a fistula can form between adjacent areas of bowel (or even between the rectal and vaginal areas). Crohn’s disease typically affects the lower part of the small intestine (ileum), but can produce inflammation and ulcerations in any part of the colon and digestive system, from the mouth to the anus. Ulcerative colitis can affect any part of the large intestine.
GETTING A PROPER DIAGNOSIS

Warning Signs of IBD:
- Bloody diarrhea
- Diarrhea that awakens you at night
- Weight loss
- Nausea and vomiting
- Abdominal pain
- Fever, fatigue
- Night sweats
- Mouth ulcers
- Ulcers in the rectal area (Crohn’s)
- Joint pain

If you have symptoms like those above, then you may have IBD or infectious gastroenteritis, but you probably don’t have irritable bowel syndrome (IBS). IBD can be difficult to diagnose and treatment may be delayed because symptoms frequently overlap with other disorders like IBS, says Christine Frissora, MD, an assistant professor of medicine at the Weill Medical College. “IBD often mimics IBS, which is a disorder that affects muscle contractions in the colon,” says Dr. Frissora. Other conditions that have similar symptoms include celiac disease or sprue (an intolerance to gluten, a protein found in wheat, rye, and barley), ovarian cysts, endometriosis, pelvic inflammatory disease, pelvic infections, and food poisoning.

The first goal is to differentiate ulcerative colitis, which affects only superficial layers of the colon, from Crohn’s disease, which causes inflammation throughout all layers of the entire GI tract. The basic work-up includes a physical exam, a stool specimen and blood sample, and either flexible sigmoidoscopy or colonoscopy (examinations of the colon with fiberoptic tubes). A biopsy of the colon and a special x-ray of the GI tract, called a barium x-ray, may also help distinguish between the two diseases.

Treating IBD now
Currently, the first line of treatment for Crohn’s are aminosalicylates, aspirin-like drugs that contain 5-aminosalicylic acid (5-ASA) such as Asacol or Colazal, and sulfasalazine (Azulfidine). They are effective in treating mild to moderate symptoms. Corticosteroids are used for moderate to severe disease. Immune modifiers including azathioprine (Imuran), 6-mercaptopurine (6-MP), cyclosporine and infliximab are reserved for ulcerative colitis patients who have not responded to aminosalicylates and corticosteroids and, for Crohn’s disease, to help decrease the dose of corticosteroids and possibly to maintain remissions.

“Because Crohn’s disease involves bacterial infection, we are now using antibiotics as part of the treatment. Probiotics may also be a useful adjunct to therapy,” remarks Dr. Scherl. Probiotics are actually supplements of live bacteria such as lactobacillus commonly found in the gut. “There are a select group of probiotics, including Culturelle, which may be very helpful.”

When medication no longer controls symptoms, surgery may become necessary. Removing the colon cures UC, but usually requires the creation of an opening in the abdomen to empty wastes into a pouch. For Crohn’s disease, surgery may allow many symptom-free years, but the disease can recur, so it’s important to be followed by a gastroenterologist.

WEBWATCH
For more information on IBD, log into:
- www.wecareinIBD.com
- Crohn’s & Colitis Foundation of America: www.ccfa.org
- American College of Gastroenterology www.acg.gi.org/acg-dev/patientinfo/ct_giproblems.html